

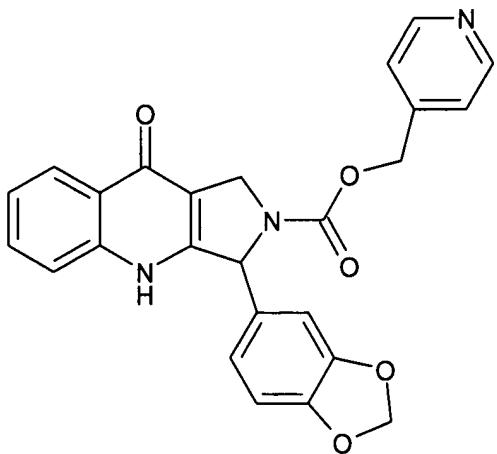
II. CLAIM AMENDMENTS

1. (Original) A method for stimulating ovarian follicular growth in a female, comprising administering to a female a medicament comprising a phosphodiesterase (PDE) inhibitor.
2. (Original) A method according to claim 1, wherein the female is undergoing ovulation induction.
3. (Original) A method according to claim 1 or 2, wherein the female is undergoing controlled ovarian hyperstimulation.
4. (Original) A method according to claim 1 or 2, wherein the medicament is administered simultaneously, separately or sequentially with FSH, or an agent having FSH activity, or an agent that stimulates endogenous FSH release.
5. (Original) A method according to claim 3, wherein the medicament is administered simultaneously, separately or sequentially with FSH, or an agent having FSH activity, or an agent that stimulates endogenous FSH release.
6. (Original) A method according to claim 4, wherein the medicament is administered with FSH, and wherein the dose of FSH is less than the dose required in the same patient in the absence of the PDE inhibitor, in order to achieve the same result in terms of follicular growth.
7. (Original) A method according to claim 5, wherein the medicament is administered with FSH, and wherein the dose of FSH is less than the dose required in the same patient in the absence of the PDE inhibitor, in order to achieve the same result in terms of follicular growth.

8. (Original) A method according to claim 1 or 2, wherein the medicament is administered starting at or about day 2 to 3 after menses.
9. (Original) A method according to claim 3, wherein the medicament is administered starting at or about day 2 to 3 after menses.
10. (Original) A method according to claim 1 or 2, wherein the medicament is administered daily until follicular growth is sufficient, when an ovulation-triggering dose of hCG is administered.
11. (Original) A method according to claim 3, wherein the medicament is administered daily until follicular growth is sufficient, when an ovulation-triggering dose of hCG is administered.
12. (Original) A method according to claim 10, wherein the ovulation-triggering dose of hCG is 5,000-10,000 IU.
13. (Original) A method according to claim 11, wherein the ovulation-triggering dose of hCG is 5,000-10,000 IU.
14. (Original) A method according to claim 1 or 2, wherein the PDE inhibitor is an inhibitor of at least one PDE type selected from 1, 5 and 6.
15. (Original) A method according to claim 3, wherein the PDE inhibitor is an inhibitor of at least one PDE type selected from 1, 5 and 6.
16. (Original) A method according to claim 1 or 2, wherein the PDE inhibitor is selected from: 5-[2-ethoxy-5-(4-methyl-1-piperazinylsulphonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (sildenafil); Zaprinast; dipyridamole; 5-(2-ethoxy-5-

morpholinoacetylphenyl)-1 -methyl-3-n-propyl-1,6-dihydro-7H-20 pyrazolo[4,3-d]pyrimidin-7-one; 3-ethyl-5-[5-(4-ethylpiperazin- 1 -ylsulphonyl)-2-n-propoxyphenyl]-2-(pyridin-2-yl) methyl-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; 3-ethyl-5-[5-(4-ethylpiperazin-1-ylsulphonyl)-2-(2-methoxyethoxy)pyridin-3-yl]-2-(pyridin-2-yl) methyl-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; (+)-3-ethyl-5-[5-(4-ethylpiperazin-1-ylsulphonyl)-2-(2-methoxy-1(R)-methylethoxy)pyridin-3-yl]-2-methyl-2,6-dihydro-7 H-pyrazolo[4 ,3-d] pyrimidin-7-one; 5-[2-ethoxy-5-(4-ethylpiperazin-1-ylsulphonyl)pyridin-3-yl]-3-ethyl-2-[2-methoxyethyl]-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; 5-[2-isobutoxy-5-(4-ethylpiperazin-1-ylsulphonyl)pyridin-3-yl]-3-ethyl-2-(1-methylpiperidin-4-yl)-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; 5-[2-ethoxy-5-(4-ethylpiperazin-1-ylsulphonyl)pyridin-3-yl]-3-ethyl-2-phenyl-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; 5-(5-acetyl-2-propoxy-3-pyridinyl)-3-ethyl-2-(1 -isopropyl-3-azetidinyl)-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; 5-(5-acetyl-2-butoxy-3-pyridinyl)-3-ethyl-2-(1-ethyl-3-azetidinyl)-2 ,6-dihydro-7H-pyrazolo [4,3-d]pyrimidin-7-one; (6R, 12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6(- 3,4-methylenedioxyphenyl)pyrazino[2',1 ':6,1]pyrido[3,4-b]indole-1,4-dione (Tadalafil; IC-351); 2-[2-ethoxy-5-(4-ethyl-piperazin-1-yl-1-sulphonyl)-phenyl]-5-methyl-7-propyl-3H-imidazo [5,1 -f][1,2,4]triazin-4-one (vardenafil); 4-bromo-5-(pyridylmethylamino)-6-[3-(4-chlorophenyl)-propoxy]-3(2H)pyridazinone; 1 -[4-[(1,3-benzodioxol-5-ylmethyl)amino]-6-chloro-2-quinozolinyl]-4-piperidine-carboxylic acid, monosodium salt; (+)-cis-5,6a,7,9,9,9a-hexahydro-2-[4-(trifluoromethyl)-phenylmethyl-5-methyl-cyclopent-[4,5]imidazo[2,1-b]purin-4(3H)one; furaciillin; cis-2-hexyl-5-methyl-3,4,5,6a,7,8,9,9a-octahydrocyclopent[4,5]-imidazo[2-,1 -b]purin-4-one; 3-acetyl-1-(2-chlorobenzyl)-2-propylindole-6- carboxylate; 3-acetyl-1 -(2-chlorobenzyl)-2-propylindole-6-carboxylate; 4-bromo-5-(3-pyridylmethylamino)-6-(3-(4-chlorophenyl)propoxy)-3-(2H)pyridazinone; 1-methyl-5(5-morpholinoacetyl-2-n-propoxyphenyl)-3-n-propyl-1,6-dihydro-7H-pyrazolo (4,3-d)pyrimidin-7-one; 1 -[4-[(1,3-benzodioxol-5-yl methyl)amino]-6-chloro-2-quinozolinyl]-4-piperidinecarboxylic acid, monosodium salt; Pharmaprojects No. 4516; Pharmaprojects No. 5051; Pharmaprojects No. 5064; Pharmaprojects No. 5069; GF-196960; E-8010 and E-4010; Bay-38-3045 & Bay-38-9456; Vinpocetine; SCH-51866; SCH-59498; (6aR,9aS)-2-(Biphenylmethyl)-5,6a,7,8,9,9a-hexahydro-5-methyl-

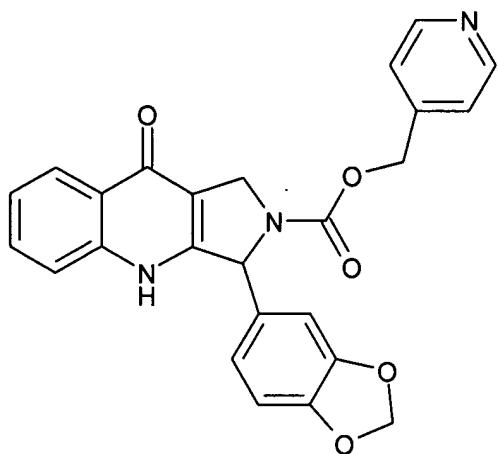
3(phenylmethyl)cyclopent [4,5] imidazo-[2,1-*b*]purin-4(3*H*)-one; 5'-Methyl-2'(biphenylylmethyl)-3'-(phenylmethyl) spiro[cyclopentane-1,7'(8'*H*)-[3*H*]imidazo[2,1-*b*]purin]-4(5'*H*)-one; (6a*R*,9a*S*)-5,6a,7,8,9,9a-Hexahydro-5-methyl-2-(phenylethynyl)-3-(phenylmethyl)cyclopent [4,5] imidazo[2,1-*b*]-purin-4(3*H*)-one; dipyridamole, AWD-12-171 and AWD-12-217; BMS-341400; UK-343,664; 5E-3623, 5E-3569, 5E-3657, E4021; KS-505a; YC-1; IDDB reference number 323951; WIN-61691; FR226807; IDDB references 461317, 462503, 461321, 461324, 466146; pyridine-4-ylmethyl 3-(1,3-benzodioxol-5-yl)-9-oxo-1,3,4,9 tetrahydro-2*H*-pyrrolo [3,4-*b*] quinoline-2-carboxylate:



17. (Original) A method according to claim 3, wherein the PDE inhibitor is selected from: 5-[2-ethoxy-5-(4-methyl-1-piperazinylsulphonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one (sildenafil); Zaprinast; dipyridamole; 5-(2-ethoxy-5-morpholinoacetylphenyl)-1-methyl-3-n-propyl-1,6-dihydro-7*H*-20 pyrazolo[4,3-*d*]pyrimidin-7-one; 3-ethyl-5-[5-(4-ethylpiperazin-1-ylsulphonyl)-2-n-propoxyphenyl]-2-(pyridin-2-yl) methyl-2,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one; 3-ethyl-5-[5-(4-ethylpiperazin-1-ylsulphonyl)-2-(2-methoxyethoxy)pyridin-3-yl]-2-(pyridin-2-yl) methyl-2,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one; (+)-3-ethyl-5-[5-(4-ethylpiperazin-1-ylsulphonyl)-2-(2-methoxy-1(R)-methylethoxy)pyridin-3-yl]-2-methyl-2,6-dihydro-7*H*-

pyrazolo[4,3-d] pyrimidin-7-one; 5-[2-ethoxy-5-(4-ethylpiperazin-1-ylsulphonyl)pyridin-3-yl]-3-ethyl-2-[2-methoxyethyl]-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; 5-[2-isobutoxy-5-(4-ethylpiperazin-1-ylsulphonyl)pyridin-3-yl]-3-ethyl-2-(1-methylpiperidin-4-yl)-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; 5-[2-ethoxy-5-(4-ethylpiperazin-1-ylsulphonyl)pyridin-3-yl]-3-ethyl-2-phenyl-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; 5-(5-acetyl-2-propoxy-3-pyridinyl)-3-ethyl-2-(1-isopropyl-3-azetidinyl)-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; 5-(5-acetyl-2-butoxy-3-pyridinyl)-3-ethyl-2-(1-ethyl-3-azetidinyl)-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; (6R, 12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxophenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione (Tadalafil; IC-351); 2-[2-ethoxy-5-(4-ethyl-piperazin-1-yl-1-sulphonyl)-phenyl]-5-methyl-7-propyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one (vardenafil); 4-bromo-5-(pyridylmethylamino)-6-[3-(4-chlorophenyl)-propoxy]-3(2H)pyridazinone; 1-[4-[(1,3-benzodioxol-5-ylmethyl)amino]-6-chloro-2-quinozolinyl]-4-piperidine-carboxylic acid, monosodium salt; (+)-cis-5,6a,7,9,9a-hexahydro-2-[4-(trifluoromethyl)-phenylmethyl]-5-methyl-cyclopent-[4,5]imidazo[2,1-b]purin-4(3H)one; furaciillin; cis-2-hexyl-5-methyl-3,4,5,6a,7,8,9,9a-octahydrocyclopent[4,5]-imidazo[2-,1-b]purin-4-one; 3-acetyl-1-(2-chlorobenzyl)-2-propylindole-6-carboxylate; 3-acetyl-1-(2-chlorobenzyl)-2-propylindole-6-carboxylate; 4-bromo-5-(3-pyridylmethylamino)-6-(3-(4-chlorophenyl)propoxy)-3-(2H)pyridazinone; 1-methyl-5-(5-morpholinoacetyl-2-n-propoxyphenyl)-3-n-propyl-1,6-dihydro-7H-pyrazolo(4,3-d)pyrimidin-7-one; 1-[4-[(1,3-benzodioxol-5-yl methyl)amino]-6-chloro-2-quinozolinyl]-4-piperidinecarboxylic acid, monosodium salt; Pharmaprojects No. 4516; Pharmaprojects No. 5051; Pharmaprojects No. 5064; Pharmaprojects No. 5069; GF-196960; E-8010 and E-4010; Bay-38-3045 & Bay-38-9456; Vinpocetine; SCH-51866; SCH-59498; (6aR,9aS)-2-(Biphenylmethyl)-5,6a,7,8,9,9a-hexahydro-5-methyl-3(phenylmethyl)cyclopent[4,5]imidazo-[2,1-b]purin-4(3H)-one; 5'-Methyl-2'(biphenylmethyl)-3'-(phenylmethyl) spiro[cyclopentane-1,7'(8'H)-[3H]imidazo[2,1-b]purin]-4(5'H)-one; (6aR,9aS)-5,6a,7,8,9,9a-Hexahydro-5-methyl-2-(phenylethynyl)-3(phenylmethyl)cyclopent[4,5]imidazo[2,1-b]purin-4(3H)-one; dipyridamole, AWD-12-171 and AWD-12-217; BMS-341400; UK-343,664; 5E-3623, 5E-3569, 5E-3657, E4021; KS-505a; YC-1; IDDB reference number 323951; WIN-61691; FR226807; IDDB references

461317, 462503, 461321, 461324, 466146; pyridine-4-ylmethyl 3-(1,3-benzodioxol-5-yl)-9-oxo-1,3,4,9 tetrahydro-2H-pyrrolo [3,4-b] quinoline-2-carboxylate:



18. (Original) A method according to claim 1 or 2, wherein the PDE inhibitor is selected from Sildenafil; Zaprinast; Dipyridamole; (6a*R*,9a*S*)-2-(Biphenylylmethyl)-5,6a,7,8,9,9a-hexahydro-5-methyl-3(phenylmethyl)cyclopent [4,5] imidazo-[2,1-*b*]purin-4(3*H*)-one; and 5'-Methyl-2'(biphenylylmethyl)-3'-(phenylmethyl) spiro[cyclopentane-1,7'(8'H)-[3*H*]imidazo[2,1-*b*]purin]-4(5'H)-one.

19. (Original) A method according to claim 3, wherein the PDE inhibitor is selected from Sildenafil; Zaprinast; Dipyridamole; (6a*R*,9a*S*)-2-(Biphenylylmethyl)-5,6a,7,8,9,9a-hexahydro-5-methyl-3(phenylmethyl)cyclopent [4,5] imidazo-[2,1-*b*]purin-4(3*H*)-one; and 5'-Methyl-2'(biphenylylmethyl)-3'-(phenylmethyl) spiro[cyclopentane-1,7'(8'H)-[3*H*]imidazo[2,1-*b*]purin]-4(5'H)-one.

20. (Original) A method according to claim 1 or 2, wherein the PDE inhibitor is Zaprinast.

21. (Original) A method according to claim 3, wherein the PDE inhibitor is Zaprinast.

22. (Original) A method according to claim 1 or 2, wherein the PDE inhibitor is Sildenafil.
23. (Original) A method according to claim 3, wherein the PDE inhibitor is Sildenafil.
24. (Original) A method according to claim 1 or 2, wherein the PDE inhibitor is Tadalafil.
25. (Original) A method according to claim 3, wherein the PDE inhibitor is Tadalafil.
26. (Original) A method according to claim 1 or 2, wherein the PDE inhibitor is a selective inhibitor of PDE 1 and PDE 5.
27. (Original) A method according to claim 3, wherein the PDE inhibitor is a selective inhibitor of PDE 1 and PDE 5.
28. (Original) A method according to claim 1 or 2, wherein the PDE inhibitor is a selective PDE 1 inhibitor.
29. (Original) A method according to claim 3, wherein the PDE inhibitor is a selective PDE 1 inhibitor.
30. (Original) A method according to claim 1 or 2, wherein the PDE inhibitor is a selective inhibitor of PDE 5.
31. (Original) A method according to claim 3, wherein the PDE inhibitor is a selective inhibitor of PDE 5.
32. (Original) A method of increasing follicle maturation comprising treating a female with a composition comprising a phosphodiesterase (PDE) inhibitor in an amount effective to stimulate follicular maturation.

33. (Cancelled)

34. (Currently Amended) A method according to claim 32 ~~or 33~~, wherein the composition comprises at least one PDE 4 inhibitor.

35. (Currently Amended) A method according to claim 32 ~~or 33~~, wherein the composition comprises at least one PDE 4 inhibitor selected from the group consisting of Piclamilast, Roflumilast, Ariflo, Filaminast, Mesopram, D4418, Arofylline, and CL1044.

36. (Currently Amended) A method according to claim 32 ~~or 33~~, wherein the composition comprises at least one PDE 4 inhibitor and one other PDE inhibitor selected from the group consisting of a PDE 1 inhibitor, a PDE 7 inhibitor, a PDE 9 inhibitor, a PDE 10 inhibitor, and a PDE 11 inhibitor.

37. (Currently Amended) A method according to claim 32 ~~or 33~~, wherein the method further comprises treatment with at least one gonadotropin selected from the group consisting of FSH, luteinizing hormone, and chorionic gonadotropin.

38. (Original) A method according to claim 34, wherein the method further comprises treatment with at least one gonadotropin selected from the group consisting of FSH, luteinizing hormone, and chorionic gonadotropin.

39. (Original) A method according to claim 35, wherein the method further comprises treatment with at least one gonadotropin selected from the group consisting of FSH, luteinizing hormone, and chorionic gonadotropin.

40. (Original) A method according to claim 36, wherein the method further comprises treatment with at least one gonadotropin selected from the group consisting of FSH, luteinizing hormone, and chorionic gonadotropin.

41. (Currently Amended) A method according to claim 32 or 33, wherein the method further comprises treatment with FSH.
42. (Currently Amended) A method according to claim 32 or 33, wherein the method further comprises administering FSH and at least one non-FSH gonadotropin hormone.
43. (Original) A method according to claim 42, wherein the non-FSH gonadotropin hormone is luteinizing hormone.
44. (Original) A method according to claim 42, wherein the non-FSH gonadotropin hormone is chorionic gonadotropin.
45. (Currently Amended) A method according to claim 32 or 33, wherein the method comprises administering a stimulator, agonist or adjuvant of FSH alone in combination with a PDE 4 inhibitor.
46. (Original) A method according to claim 45, wherein the stimulator of FSH is selected from the group consisting of Letrozole, Anastrozole, and Vorozole.
47. (Original) A method according to claim 37, wherein the PDE inhibitor and the gonadotropin hormone are administered concurrently.
48. (Original) A method according to claim 37, wherein the PDE 4 inhibitor and FSH are contained in a single vial as a mixture.
49. (Cancelled)
50. (Original) A method according to claim 37, wherein the PDE inhibitor is administered prior to the gonadotropin hormone treatment.

51. (Original) A method according to claim 37, wherein the PDE inhibitor is administered after the gonadotropin hormone treatment.
52. (Original) A method according to claim 37, wherein the FSH is administered at a dosage range of about 5 to 450 IU/day.
53. (Original) A method according to claim 37, wherein the FSH is administered at a dosage range of about 5 to 75 IU/day.
54. (Original) A method according to claim 32, wherein the method comprises administering to the female a composition comprising at least one PDE 4 inhibitor and an exogenous FSH hormone.
55. (Original) A method according to claim 54, wherein the exogenous FSH hormone is a recombinant FSH hormone.
56. (Original) A method according to claim 54, wherein the exogenous FSH hormone is urinary FSH hormone.
57. (Original) A method according to claim 54, wherein the PDE 4 inhibitor is administered in a dose of about 0.05 mg/day to about 5 mg/day.
58. (Original) A method according to claim 54, wherein the PDE 4 inhibitor is administered in a dose of about 10 mg/day to about 200 mg/day.
59. (Original) A method according to claim 54, wherein the FSH is administered in a dosage range of 5 IU FSH/day to 75 IU FSH/day.

60. (Original) A method according to claim 54, wherein the FSH is administered in a dosage of 150 IU FSH per day.

61. (Original) A method according to claim 54, wherein the FSH is administered in a single dose.

62. (Original) A method according to claim 54, wherein the FSH is administered in multiple doses.

63. (Original) A method according to claim 54, wherein the FSH is administered intramuscularly or subcutaneously.

64. (Original) A method according to claim 54, wherein the FSH is administered between day 2 and day 14 of the menstrual cycle of the female.

65. (Original) A method according to claim 54, wherein the FSH is administered for 7 to 12 consecutive days.

66. (Original) A method according to claim 54, wherein the method further comprises suppression of endogenous FSH and LH production in the female prior to administration of the PDE 4 inhibitor and the FSH hormone.

67. (Original) A method according to claim 66, wherein suppression of endogenous FSH and LH production is effected by the administration of GnRH or an analog thereof to the female.

68. (Original) A method according to claim 66, wherein GnRH, or an analog thereof, is administered to the female for 30 days prior to the administration of the at least one PDE 4 inhibitor and the exogenous FSH hormone.

69. (Original) A method according to claim 67, wherein GnRH, or an analog thereof, is administered in a dosage range of from about 0.25 mg to about 3 mg GnRH on a daily basis.

70. (Original) A method according to claim 54, wherein the female produces 4 or more oocytes that are harvestable.

71. (Original) A method according to claim 70, further comprising the step of harvesting the oocytes 12 days after the PDE 4 inhibitor and the FSH were first administered.

72. (Original) A method according to claim 71, further comprising the step of fertilizing the harvested oocytes in vitro, culturing the harvested, fertilized oocytes to the 4-8 cell stage, and transferring the 4-8 cell stage fertilized oocytes to the uterus of a mammal.

Claims 73-78 (Cancelled)